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January 20, 2004
Date

Steven L. Highlander

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Paul McCray *et al.*

Serial No.: 09/448,613

Filed: November 22, 1999

For: METHODS AND COMPOSITIONS FOR INCREASING THE INFECTIVITY OF GENE TRANSFER VECTORS

Group Art Unit: 1641

Examiner: R. Schnizer

Atty. Dkt. No.: IOWA:022/SLH

RESPONSE TO INTERVIEW SUMMARY

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-01450

Sir:

This paper is submitted in response to the Interview Summary mailed on December 19, 2003, the deadline for response being January 20, 2004, since January 19, 2004 is a holiday. No fees are believed due; however, should any fees be due for any reason relating to this paper, applicants authorize the Commissioner to debit Fulbright & Jaworski Deposit Account No. 55-1212/IOWA:022US/SLH.

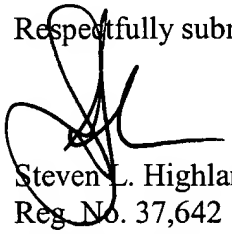
REMARKS

Applicants agree with and adopt fully the examiner's summary of the December 11, 2003 interview as indicated in the Notice of Allowability mailed on December 19, 2003.

However, applicants note that claim 67, which has not been withdrawn or canceled, is not indicated as allowed on the Notice of Allowability (see attached summary of claims). Applicants respectfully request clarification, and hopefully allowance, of this claim.

Should Examiner Schnizer have any questions regarding this response, he is invited to contact the undersigned attorney at (512) 536-3184 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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Date: January 20, 2004

Summary of Pending Claims for USSN 09/448,613

1. A method for increasing infection viral vector infection of epithelial cells in an epithelial tissue comprising:

(a) contacting said epithelial tissue with a composition that comprises a hypotonic solution and/or a chelator of divalent cations in an amount sufficient to produce permeabilized epithelial tissue; and

(b) contacting permeabilized epithelial cells with a viral vector;

whereby an increase in transepithelial permeability increases viral vector infection of said epithelial cells.

2. The method of claim 1, wherein said epithelial cells are in airway epithelial tissue.

3. The method of claim 2, wherein said airway epithelial tissue is bronchial or bronchiolar tissue.

4. The method of claim 2, wherein said airway epithelial tissue is tracheal tissue.

5. The method of claim 2, wherein said airway epithelial tissue is alveolar tissue.

6. The method of claim 1, further comprising increasing the proliferation of said epithelial cells.

7. The method of claim 6, wherein increasing the proliferation of said epithelial cells is achieved by contacting said cells with a proliferative factor.

8. The method of claim 7, wherein said proliferative factor is a growth factor.

10. The method of claim 1, wherein said composition comprises a hypotonic solution.

11. The method of claim 1, wherein said composition comprises a chelator of divalent cations.

12. The method of claim 11, wherein said chelator of divalent cations is EGTA, BAPTA or EDTA.

26. The method of claim 1, further comprising, infecting said epithelial cells in said permeabilized tissue with a virus vector selected from the group consisting of a retrovirus, a lentivirus, an adenovirus, an adeno-associated virus, a parvovirus, a papovavirus, paramyxovirus and a vaccinia virus.

27. The method of claim 26, wherein the virus vector comprises a non-viral gene under the control of a promoter active in eukaryotic cells.

28. The method of claim 27, wherein said non-viral gene is a human gene.

29. The method of claim 28, wherein said gene encodes a polypeptide selected from the group consisting of a tumor suppressor, a cytokine, an enzyme, a toxin, a growth factor, a membrane channel, an inducer of apoptosis, a transcription factor, a hormone and a single chain antibody.

30. The method of claim 26, wherein the virus vector is a replication-defective virus.

31. The method of claim 30, wherein the virus vector is a retroviral vector.

32. The method of claim 1, wherein said epithelial tissue is diseased.

33. The method of claim 32, wherein said disease is lung cancer, tracheal cancer, asthma, surfactant protein B deficiency, alpha-1-antitrypsin deficiency or cystic fibrosis.

34. The method of claim 7, wherein said proliferative factor is delivered as an aerosol.

35. The method of claim 7, wherein said proliferative factor is delivered as a topical solution.

36. The method of claim 1, wherein said composition is delivered as an aerosol.

37. The method of claim 1, wherein said composition is delivered as a topical solution.

48. An *in vivo* method for redistributing viral receptors on an epithelial cell of an epithelial tissue from the basolateral side to the apical side of said epithelial cell comprising increasing the transepithelial permeability of said epithelial tissue by contacting said epithelial tissue with a hypotonic solution and/or a chelator of divalent cations, whereby increased transepithelial permeability facilitates redistribution of said viral receptors on said epithelial cell.

49. The method of claim 48, wherein said receptor is a retroviral receptor.

50. A method for expressing a polypeptide in cells of an epithelial tissue comprising:

(a) providing a packaged viral vector comprising a polynucleotide encoding said polypeptide;

(b) increasing the permeability of said epithelial tissue by treating said tissue with a hypotonic solution and/or a chelator of divalent cations; and

(c) contacting cells of the permeablized epithelial tissue with said packaged viral vector under conditions permitting the uptake of said packaged viral vector by said cells and expression of said polypeptide therein; and

whereby increased permeability of said epithelial tissue facilitates improved viral transduction of said cells, which in turn facilitates expression of said polypeptide.

51. The method of claim 50, further comprising increasing the proliferation of cells of said epithelial tissue.

52. The method of claim 50, wherein said viral vector is a retroviral vector.

53. A method of increasing transport of chloride ions in airway epithelial tissue of a mammal suffering from cystic fibrosis comprising:

a) providing a packaged viral vector comprising a polynucleotide encoding a cystic fibrosis transmembrane regulator (CFTR) protein;

b) contacting said airway epithelial tissue with a hypotonic solution and/or a chelator of divalent cations in a sufficient amount to produce permeabilized epithelial tissue;

c) contacting cells of said permeablilized airway epithelial tissue with said packaged viral vector under conditions permitting uptake of the packaged viral vector by said cells, and expression of said CFTR protein therein;

wherein a sufficient quantity of said CFTR protein is produced to increase chloride ion transport in the airway epithelial tissue.

54. The method of claim 53, further comprising increasing the proliferation of cells of said pithelial tissue.

56. The method of claim 53, wherein said airway tissue is alveolar tissue, bronchial tissue or tracheal tissue.

66. The method of claim 54, wherein increasing the proliferation of cells of said diseased epithelial tissue comprises contacting said cells with a proliferative agent.

67. The method of claim 53, wherein said viral vector is a retroviral vector.

70. A method for transducing epithelial cells with a viral vector comprising delivering to said epithelial cells a packaged viral vector and EGTA in a hypotonic solution.

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January 20, 2004

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Steven L. Highlander

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Re: Serial Number 09/448,613 entitled "METHODS AND COMPOSITIONS FOR INCREASING THE INFECTIVITY OF GENE TRANSFER VECTORS" by Paul B. McCray, Jr. et al.
Our ref: IOWA:022US / Matter No. 10008931

Commissioner:

Enclosed for filing in the above-referenced patent application is:

1. Interview Summary;

2. A return postcard to acknowledge receipt of these materials. Please date stamp and mail this postcard.

Should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to the enclosed materials, the Commissioner is authorized to deduct said fees from Fulbright & Jaworski L.L.P. Account No.: 50-1212/IOWA:22US/SLH.

Very truly yours,

Steven L. Highlander

SLH/cpj
Encl: As noted
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